UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/661,927	09/14/2000	William J. Dower	019282-000110US	1158

20350 7590 07/22/2002

TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER
EPPERSON, JON D

ART UNIT	PAPER NUMBER
1627	

DATE MAILED: 07/22/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
File Copy	09/661,927	DOWER ET AL.	
	Examiner	Art Unit	
	Jon D Epperson	1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 May 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-137* is/are pending in the application.

4a) Of the above claim(s) *69-137* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-68* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Please Note: In an effort to enhance communication with our customers and reduce processing time, Group 1627 is running a Fax Response Pilot for Written Restriction Requirements. A dedicated Fax machine is in place to receive your responses. The fax number is 703-308-4315. A fax cover sheet is attached to this Office Action for your convenience. We encourage your participation in this Pilot program. If you have any questions or suggestions please contact Jyothsna Venkat, Supervisory Patent Examiner, at (703) 308-2439. Thank you in advance for allowing us to enhance our customer service. Please limit the use of this dedicated Fax number to responses to Written Restrictions.

1. Please note: There is a change in Examiner handling prosecution in the current case from Examiner Steven C. Tizio to Jon D. Epperson.

2. The Response to the Restriction Requirement submitted by applicant dated May 17, 2002, is acknowledged. Claims 25, 26, 43, 53 and 55 were amended and no claims were added or cancelled.

3. Applicant's election, with traverse, of Group I (claims 1-68) is acknowledged in Paper No. 7. Applicant's election of species is also acknowledged in Paper No. 7. The traversal will be addressed in the first action on the merits.

4. Claims 69-137 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions, the requirement having been traversed in Paper No. 7.

5. Therefore, claims 1-68 are examined on the merits in this action. However, upon further review of the instant case, additional restrictions were deemed necessary and appropriate as specified below. Furthermore, the previous species election (see paper number 7, "Response to Species Election Requirement") has been withdrawn. A new species election is required for the groups listed below (see paragraphs 11-29).

Election/Restriction

6. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I Claims 1 (in part), 2 (in part), 3 and 5 drawn to a first method for "screening for a carrier-type transport protein and/or a ligand thereto" wherein the complex is "internalized within the cell" and wherein "the reporter contains a cleavable site and the reporter is cleaved at the cleavable site after the complex is internalized within the cell." The invention is classified variously, for example, in class 436, subclass 501; class 435, subclass 7.1; class 435, DIG 2+ (depending on the type of ligand).

II Claims 1 (in part), 2 (in part) and 4 drawn to a second method for "screening for a carrier-type transport protein and/or a ligand thereto" wherein the complex is "internalized within the cell" and wherein the "reporter comprises an agent that causes a morphological change upon internalization within a cell ... [and]

the agent triggers a detectable morphological change in the cell." The invention is classified variously, for example, in class 436, subclass 501; class 435, subclass 7.1; class 435, DIG 2+ (depending on the type of ligand).

III Claims 1 (in part), 2 (in part), and 6-11 drawn to a third method for "screening for a carrier-type transport protein and/or a ligand thereto" wherein the complex is "internalized within the cell" and "the reporter comprises a fluorophore and a quencher moiety." The invention is classified variously, for example, in class 436, subclass 501; class 435, subclass 7.1; class 435, DIG 2+ (depending on the type of ligand).

IV Claims 1 (in part), 2 (in part) and 12-13 drawn to a fourth method for "screening for a carrier-type transport protein and/or a ligand thereto" wherein the complex is "internalized within the cell" and wherein "the receptor comprises a detection moiety disposed to interact with an intracellular agent." The invention is classified variously, for example, in class 436, subclass 501; class 435, subclass 7.1; class 435, DIG 2+ (depending on the type of ligand).

V Claims 1 (in part), 2 (in part) and 14-18 drawn to a fifth method for "screening for a carrier-type transport protein and/or a ligand thereto" wherein the complex is "internalized within the cell" and wherein "the reporter comprises a substrate for an enzyme." The

invention is classified variously, for example, in class 436, subclass 501; class 435, subclass 7.1; class 435, DIG 2+ (depending on the type of ligand).

VI Claims 1 (in part), 2 (in part) and 19 drawn to a sixth method for "screening for a carrier-type transport protein and/or a ligand thereto" wherein the complex is "internalized within the cell" and wherein "the reporter promotes aggregation of subunits of a multimeric enzyme expressed within the population of cells." The invention is classified variously, for example, in class 436, subclass 501; class 435, subclass 7.1; class 435, DIG 2+ (depending on the type of ligand).

VII Claims 1 (in part), 2 (in part) and 20-21 drawn to a seventh method for "screening for a carrier-type transport protein and/or a ligand thereto" wherein the complex is "internalized within the cell" and wherein "the reporter promotes transcription from a promoter within a cell resulting in expression of an expression product." The invention is classified variously, for example, in class 436, subclass 501; class 435, subclass 7.1; class 435, DIG 2+ (depending on the type of ligand).

VIII Claims 1 (in part), 2 (in part) and 22 drawn to an eighth method for "screening for a carrier-type transport protein and/or a ligand thereto" wherein the complex is "internalized within the cell" and

wherein "the reporter confers a selective advantage within the cell(s)." The invention is classified variously, for example, in class 436, subclass 501; class 435, subclass 7.1; class 435, DIG 2+ (depending on the type of ligand).

IX Claims 1 (in part) and 23 drawn to a ninth method for "screening for a carrier-type transport protein and/or a ligand thereto" wherein "the method further comprises washing cells to remove unincorporated complexes before the detecting step, whereby the signal from reporter internalized within the cell is preferentially detected." The invention is classified variously, for example, in class 436, subclass 501; class 435, subclass 7.1; class 435, DIG 2+ (depending on the type of ligand).

X Claims 1 (in part) and 24 drawn to a tenth method for "screening for a carrier-type transport protein and/or a ligand thereto" wherein "the method further comprises contacting cells with a fluorescence quencher incapable of entering the cells to quench fluorescence of unincorporated complexes before the detecting step, whereby signal from reporter internalized within the cell is preferentially detected." The invention is classified variously, for example, in class 436, subclass 501; class 435, subclass 7.1; class 435, DIG 2+ (depending on the type of ligand).

XI Claims 1 (in part), 25 (in part), 26 drawn to an eleventh method for "screening for a carrier-type transport protein and/or a ligand thereto" wherein "the population of cells comprise different cells that are located in a single reaction vessel" and wherein "the different cells comprise test cells and counterpart control cells, the test cell expressing one of the one or more carrier-type transport proteins while the control cells fail to express the transport protein expressed by the test cells." The invention is classified variously, for example, in class 436, subclass 501; class 435, subclass 7.1; class 435, DIG 2+ (depending on the type of ligand).

XII Claims 1 (in part), 25 (in part), 27 drawn to a twelfth method for "screening for a carrier-type transport protein and/or a ligand thereto" wherein "the population of cells comprise different cells that are located in a single reaction vessel" and wherein "the different cells comprise test cells and counterpart control cells, the test cell expressing one of the one or more carrier-type transport proteins while the control cells fail to express the transport protein expressed by the test cells." The invention is classified variously, for example, in class 436, subclass 501; class 435, subclass 7.1; class 435, DIG 2+ (depending on the type of ligand).

XIII Claims 1 (in part), 25 (in part), 28 (in part), 29 drawn to a thirteenth method for "screening for a carrier-type transport protein

and/or a ligand thereto" wherein "the population of cells comprise different cells that are located in a single reaction vessel" and wherein "determining the identity of the cell to which the at least one complex is bound or internalized within from its distinguishable characteristic" and wherein "the distinguishable characteristics are different cellular morphologies." The invention is classified variously, for example, in class 436, subclass 501; class 435, subclass 7.1; class 435, DIG 2+ (depending on the type of ligand).

XIV Claims 1 (in part), 25 (in part), 28 (in part), 30 drawn to a fourteenth method for "screening for a carrier-type transport protein and/or a ligand thereto" wherein "the population of cells comprise different cells that are located in a single reaction vessel" and wherein "determining the identity of the cell to which the at least one complex is bound or internalized within from its distinguishable characteristic" and wherein "the distinguishable characteristics are different stains on the cell." The invention is classified variously, for example, in class 436, subclass 501; class 435, subclass 7.1; class 435, DIG 2+ (depending on the type of ligand).

XV Claims 1 (in part), 25 (in part), 28 (in part), 31-34 drawn to a fifteenth method for "screening for a carrier-type transport protein

and/or a ligand thereto" wherein "the population of cells comprise different cells that are located in a single reaction vessel" and wherein "determining the identity of the cell to which the at least one complex is bound or internalized within from its distinguishable characteristic" and wherein "the distinguishable characteristics are different markers located at the surface of the cells." The invention is classified variously, for example, in class 436, subclass 501; class 435, subclass 7.1; class 435, DIG 2+ (depending on the type of ligand).

XVI Claims 1 (in part), 35 (in part) and 36 drawn to a sixteenth method for "screening for a carrier-type transport protein and/or a ligand thereto" wherein the method further comprises "contacting the cells within the reaction vessel with a plurality of different complexes" and wherein the method further comprises "separately contacting the population of cells within different reaction vessels with the different complexes such that cells within the same reaction vessel receive the same complex while cells in at least some of the different reaction vessels receive different complexes." The invention is classified variously, for example, in class 436, subclass 501; class 435, subclass 7.1; class 435, DIG 2+ (depending on the type of ligand).

XVII Claims 1 (in part), 35 (in part) and 37-40 drawn to a seventeenth method for "screening for a carrier-type transport protein and/or a ligand thereto" wherein the "the reporter varies between different complexes and different reporters are disposed to generate different signals." The invention is classified variously, for example, in class 436, subclass 501; class 435, subclass 7.1; class 435, DIG 2+ (depending on the type of ligand).

XVIII Claims 1 (in part), 41 (in part), 42 (in part), 43 (in part) and 44 drawn to an eighteenth method for "screening for a carrier-type transport protein and/or a ligand thereto" wherein "the compound complexed to the internalized complex being a substrate potentially able to transport an agent into cells expressing a carrier type transport protein, the method further comprising: (e) providing a modified complex, the modified complex comprising the compound identified in the detecting step (d) and an agent; (f) contacting one or more cells with the modified complex; and determining whether the modified complex is internalized within one of the one or more cells by detecting the modified complex within the one or more cells, such detection providing an indication that the compound can serve as a substrate for transporting agents into cells expressing carrier-type transport proteins" and "wherein the providing step [of claim 43] comprises

synthesizing the modified complex." The invention is classified variously, for example, in class 436, subclass 501; class 435, subclass 7.1; class 435, DIG 2+ (depending on the type of ligand).

XIX Claims 1 (in part), 41 (in part), 42 (in part), 43 (in part) and 45 drawn to a nineteenth method for "screening for a carrier-type transport protein and/or a ligand thereto" wherein "the compound complexed to the internalized complex being a substrate potentially able to transport an agent into cells expressing a carrier type transport protein, the method further comprising: (e) providing a modified complex, the modified complex comprising the compound identified in the detecting step (d) and an agent; (f) contacting one or more cells with the modified complex; and determining whether the modified complex is internalized within one of the one or more cells by detecting the modified complex within the one or more cells, such detection providing an indication that the compound can serve as a substrate for transporting agents into cells expressing carrier-type transport proteins" and "the modified complex further comprises a reporter attached at a site other than the attachment site." The invention is classified variously, for example, in class 436, subclass 501; class 435, subclass 7.1; class 435, DIG 2+ (depending on the type of ligand).

XX Claims 1 (in part) and 46 drawn to a twentieth method for "screening for a carrier-type transport protein and/or a ligand thereto" wherein the method further comprises "providing a focused library, the focused library comprising a plurality of complexes, each complex in the focused library comprising a compound that is a variant of the compound identified in step (e)." The invention is classified variously, for example, in class 436, subclass 501; class 435, subclass 7.1; class 435, DIG 2+ (depending on the type of ligand).

XXI Claims 1 (in part) and 47-48 drawn to a twenty first method for "screening for a carrier-type transport protein and/or a ligand thereto" wherein "the population of cells has been transformed with a DNA library encoding the one or more transport proteins." The invention is classified variously, for example, in class 436, subclass 501; class 435, subclass 7.1; class 435, DIG 2+ (depending on the type of ligand).

XXII-XXXIV Claims 1 (in part), 49 (in part), 50-52 (in part), 55-67 (in part) drawn to more methods for "screening for a carrier-type transport protein and/or a ligand thereto" wherein "the carrier-type transport protein is" an "amino acid transporter" (Group XXII, see claim 49), a "dipeptide transporter" (Group XXIII, see claim 49), a "oligopeptide transporter" (Group XXIV, see claim 49), a "simple

sugar transporter" (Group XXV, see claim 49), a "bile acid transporter" (Group XXVI, see claim 49), a "vitamin transporter" (Group XXVII, see claim 49), a "phosphate transporter" (Group XXVIII, see claim 49), a "monocarboxylic acid transporter" (Group XXIX, see claim 49), an "organic anion transporter" (Group XXX, see claim 49), an "organic cation transporter" (Group XXXI, see claim 49), a "fatty acid transporter" (Group XXXII, see claim 49), a "nucleoside transporter" (Group XXXIII, see claim 49) and an "a ABC transporter" (Group XXXIV, see claim 49). The invention is classified variously, for example, in class 436, subclass 501; class 435, subclass 7.1; class 435, DIG 2+ (depending on the type of ligand).

XXXV Claims 1 (in part), 53-54 drawn to a thirty fifth method for "screening for a carrier-type transport protein and/or a ligand thereto" wherein "the cells are treated to yield membrane preparations or vesicles and the complexes are contacted with the membrane preparations or vesicles." The invention is classified variously, for example, in class 436, subclass 501; class 435, subclass 7.1; class 435, DIG 2+ (depending on the type of ligand).

XXXVI Claims 1 (in part), 68 drawn to a thirty sixth method for "screening for a carrier-type transport protein and/or a ligand thereto" wherein the method further comprises using control cells repeatedly. The

invention is classified variously, for example, in class 436, subclass 501; class 435, subclass 7.1; class 435, DIG 2+ (depending on the type of ligand).

7. The inventions are distinct, each from the other because of the following reasons:

8. Groups I-XXXVI represent patentably distinct methods. The methods are distinct because they use different steps, require different reagents and/or will produce different results (they will screen different classes of molecules). In the instant case, each Group i.e., Groups I-XXXVI, will require different reagents and, as a result, will also require different method steps. For example, Group II will require different reagents (materials that will trigger morphological changes in the cell) than Group III (materials for fluorescence detection i.e., a fluorophore and a quencher moiety). As a result, Groups II and III will require different method steps i.e., Group II will require method steps for the production and use of materials that will trigger morphological changes and also method steps for the detection of those morphological changes, whereas Group III will require method steps for the production and use of the fluorophore and quencher moiety and method steps (and equipment) for the detecting the degree of quenching of the fluorophore. Furthermore, the method steps of Group III will produce different results than the method steps of Group II in situations where the materials of Group III (fluorophore and quencher) are required. The patentably distinct features for the other Groups i.e., Groups I-XXXVI are listed above in paragraph 6. Consequently, examining Groups I-XXXVI together will require searching different reagents, different method steps, and/or different resulting products, which in

most cases will fall under many different US classification numbers (see paragraph 6 above). Therefore, searching Groups I-XXXVI together would represent an undue search burden. In addition, art anticipating or rendering obvious each Group i.e., Groups I-XXXVI would not render obvious another group, because they are drawn to different inventions that have different distinguishing features and/or characteristics (e.g., a demonstrated ability to screen for a ligand and/or complex to a sugar transporter (Group XXV) would not render obvious an ability to screen for a fatty acid transporter (Group XXXII). Each group will support separate patents. Consequently, Groups I-XXXVI have different issues regarding patentability and enablement and represent patentably distinct subject matter.

9. These inventions have acquired a separate status in the art as shown by their different classification and/or divergent subject matter. The different methods and products would require completely different searches in both the patent and non-patent databases, and there is no expectation that the searches would be coextensive. Therefore, this does create an undue search burden, and restriction for examination purposes as indicated is proper.

10. These inventions have acquired a separate status in the art as shown by their different classification and/or divergent subject matter. The different methods and products would require completely different searches in both the patent and non-patent databases, and there is no expectation that the searches would be coextensive. Therefore, this does create an undue search burden, and restriction for examination purposes as indicated is proper.

11. This application contains claims directed to the following patentably distinct species of the claimed inventions as set forth below.

12. If applicant elects ***any*** of the invention from Groups I-XXXVI applicant is required to elect from the following patentably distinct species. Claims 1 is generic.

Subgroup 1: Species of Reporter and Linker (see claim 1)

For the purposes of search, applicant is required to elect a ***single species*** of "reporter" in step "1a" of claim 1 wherein a ***specific structure*** is set forth, which clearly shows all of the atoms and bonds that are necessary to define the reporter including ***everything the reporter comprises*** and including all attachment points including all atoms and bonds for the "linker" moiety if present. Applicant should ***not*** use notations like X or R when identifying the elected structure because these letters represent groups with variable members and, as a result, more than one species would be erroneously elected. Furthermore, applicant ***must*** disclose which claims read on the elected "reporter." Applicant ***must not*** group all elected species together (i.e., Subgroups 1-24) and then disclose which claims read on the sum total of the elected species. Applicant ***must*** disclose which claims read **ONLY** on the elected "reporter" (i.e., what groups read ONLY on Subgroup 1).

Subgroup 2: Species of cells (see claim 1)

A ***specific single species*** *of* cells must be elected for the purposes of a search. Furthermore, applicant ***must*** disclose which claims read on the elected "reporter." Applicant ***must not*** group all elected species together (i.e., Subgroups 1-24) and then disclose which claims read on the sum total of the elected species. Applicant ***must*** disclose which claims read **ONLY** on the elected "cells" (i.e., what groups read ONLY on Subgroup 2).

Subgroup 3: Species of carrier-type transport protein (see claim 1)

A ***specific single species*** *of* carrier-type transport protein must be elected for the purposes of a search. Furthermore, applicant ***must*** disclose which claims read on the elected "carrier-type transport protein." Applicant ***must not*** group all elected species together (i.e., Subgroups 1-24) and then disclose which claims read on the sum total of the elected

species. Applicant ***must*** disclose which claims read **ONLY** on the elected "carrier-type transport protein" (i.e., what groups read ONLY on Subgroup 3).

Subgroup 4: Species of detecting a signal (see claim 1)

A ***specific single species*** *of* method for "detecting a signal" must be elected for the purposes of a search. Furthermore, applicant ***must*** disclose which claims read on the elected method for "detecting a signal." Applicant ***must not*** group all elected species together (i.e., Subgroups 1-24) and then disclose which claims read on the sum total of the elected species. Applicant ***must*** disclose which claims read **ONLY** on the elected method for "detecting a signal" (i.e., what groups read ONLY on Subgroup 4).

Subgroup 5: Species of complex interaction (see claim 1)

A. Complex is bound to a cell
B. Complex is internalized within a cell

13. If applicant elects the invention of Group I, applicant is ***further required*** to elect from the following patentably distinct species (note applicant must also elect Species in Subgroups 1-5 in paragraph 12). Claim 1 is generic.

Subgroup 6: Species of protein (see claim 5)

A ***specific single species*** *of* "agent inhibition" must be elected for the purposes of a search e.g., cytoskeleton formation inhibition. Furthermore, applicant ***must*** disclose which claims read on the elected "agent inhibition." Applicant ***must not*** group all elected species together (i.e., Subgroups 1-24) and then disclose which claims read on the sum total of the elected species. Applicant ***must*** disclose which claims read **ONLY** on the elected "agent inhibition" (i.e., what groups read ONLY on Subgroup 6).

14. If applicant elects the invention of Group II, applicant is ***further required*** to elect from the following patentably distinct species (note applicant must also elect Species in Subgroups 1-5 in paragraph 12). Claim 1 is generic.

Subgroup 7: Species of protein (see claim 4)

A ***specific single species*** *of* "morphological change" must be elected for the purposes of a search. Furthermore, applicant ***must*** disclose which claims read on the elected "morphological change." Applicant ***must not*** group all elected species together (i.e., Subgroups 1-24) and then disclose which claims read on the sum total of the elected species. Applicant ***must*** disclose which claims read **ONLY** on the elected "morphological change" (i.e., what groups read ONLY on Subgroup 8).

15. If applicant elects the invention of Group III, applicant is ***further required*** to elect from the following patentably distinct species (note applicant must also elect Species in Subgroups 1-5 in paragraph 12). Claim 1 is generic.

Subgroup 8: Species of enzyme (see claim 8)

A ***specific single species*** *of* enzyme must be elected for the purposes of a search. Furthermore, applicant ***must*** disclose which claims read on the elected "enzyme." Applicant ***must not*** group all elected species together (i.e., Subgroups 1-24) and then disclose which claims read on the sum total of the elected species. Applicant ***must*** disclose which claims read **ONLY** on the elected "enzyme" (i.e., what groups read ONLY on Subgroup 8).

Subgroup 9: Species of enzyme type (see claims 9 and 10)

A. Endogenous

B. Expressed from an exogenous sequence

16. If applicant elects the invention of Group IV, applicant is ***further required*** to elect from the following patentably distinct species (note applicant must also elect Species in Subgroups 1-5 in paragraph 12). Claim 1 is generic.

Subgroup 10: Species of intracellular agent (see claim 12)

A ***specific single species*** *of* intracellular agent must be elected for the purposes of a search. Furthermore, applicant ***must*** disclose which claims read on the elected "intracellular agent." Applicant ***must not*** group all elected species together (i.e., Subgroups 1-24) and then disclose which claims read on the sum total of the elected species. Applicant ***must*** disclose which claims read **ONLY** on the elected "intracellular agent" (i.e., what groups read ONLY on Subgroup 10).

17. If applicant elects the invention of Group V, applicant is ***further required*** to elect from the following patentably distinct species (note applicant must also elect Species in Subgroups 1-5 in paragraph 12). Claim 1 is generic.

Subgroup 11: Species of enzyme (see claims 15-18)

A ***specific single species*** *of* enzyme must be elected for the purposes of a search. Furthermore, applicant ***must*** disclose which claims read on the elected "enzyme." Applicant ***must not*** group all elected species together (i.e., Subgroups 1-24) and then disclose which claims read on the sum total of the elected species. Applicant ***must*** disclose which claims read **ONLY** on the elected "enzyme" (i.e., what groups read ONLY on Subgroup 11).

18. If applicant elects the invention of Group VI, applicant is ***further required*** to elect from the following patentably distinct species (note applicant must also elect Species in Subgroups 1-5 in paragraph 12). Claim 1 is generic.

Subgroup 12: Species of enzyme (see claim 19)

A ***specific single species*** *of* enzyme must be elected for the purposes of a search. Furthermore, applicant ***must*** disclose which claims read on the elected "enzyme." Applicant ***must not*** group all elected species together (i.e., Subgroups 1-24) and then disclose which claims read on the sum total of the elected species. Applicant ***must*** disclose which claims read **ONLY** on the elected "enzyme" (i.e., what groups read ONLY on Subgroup 12).

19. If applicant elects the invention of Group VII, applicant is ***further required*** to elect from the following patentably distinct species (note applicant must also elect Species in Subgroups 1-5 in paragraph 12). Claim 1 is generic.

Subgroup 13: Species of expression product (see claim 20)

A ***specific single species*** *of* expression product must be elected for the purposes of a search. Furthermore, applicant ***must*** disclose which claims read on the elected "expression product." Applicant ***must not*** group all elected species together (i.e., Subgroups 1-24) and then disclose which claims read on the sum total of the elected species. Applicant ***must*** disclose which claims read **ONLY** on the elected "expression product" (i.e., what groups read ONLY on Subgroup 13).

Subgroup 14: Species of detectable signal (see claim 21)

A ***specific single species*** *of* detectable signal must be elected for the purposes of a search. Furthermore, applicant ***must*** disclose which claims read on the elected "detectable signal." Applicant ***must not*** group all elected species together (i.e., Subgroups 1-24) and then disclose which claims read on the sum total of the elected species. Applicant ***must*** disclose which claims read **ONLY** on the elected "detectable signal" (i.e., what groups read ONLY on Subgroup 14).

Subgroup 15: Species of enzyme (see claim 21)

A ***specific single species*** *of* enzyme must be elected for the purposes of a search e.g., cytoskeleton formation inhibition. Furthermore, applicant ***must*** disclose which claims read on the elected "enzyme." Applicant ***must not*** group all elected species together (i.e., Subgroups 1-24) and then disclose which claims read on the sum total of the elected species. Applicant ***must*** disclose which claims read **ONLY** on the elected "enzyme" (i.e., what groups read ONLY on Subgroup 15).

20. If applicant elects the invention of Group VIII, applicant is ***further required*** to elect from the following patentably distinct species (note applicant must also elect Species in Subgroups 1-5 in paragraph 12). Claim 1 is generic.

Subgroup 16: Species of selective advantage (see claim 22)

A ***specific single species*** *of* selective advantage must be elected for the purposes of a search. Furthermore, applicant ***must*** disclose which claims read on the elected "selective advantage." Applicant ***must not*** group all elected species together (i.e., Subgroups 1-24) and then disclose which claims read on the sum total of the elected species. Applicant ***must*** disclose which claims read **ONLY** on the elected "selective advantage" (i.e., what groups read ONLY on Subgroup 16).

Subgroup 17: Species of conditions that enrich (see claim 22)

A ***specific single species*** *of* conditions that enrich must be elected for the purposes of a search. Furthermore, applicant ***must*** disclose which claims read on the elected "conditions that enrich." Applicant ***must not*** group all elected species together (i.e., Subgroups 1-24) and then disclose which claims read on the sum total of the elected species. Applicant ***must*** disclose which claims read **ONLY** on the elected "conditions that enrich" (i.e., what groups read ONLY on Subgroup 17).

21. If applicant elects the invention of Group X, applicant is ***further required*** to elect from the following patentably distinct species (note applicant must also elect Species in Subgroups 1-5 in paragraph 12). Claim 1 is generic.

Subgroup 18: Species of fluorescence quencher (see claim 24)

A ***specific single species*** *of* fluorescence quencher must be elected for the purposes of a search. Furthermore, applicant ***must*** disclose which claims read on the elected "fluorescence quencher." Applicant ***must not*** group all elected species together (i.e., Subgroups 1-24) and then disclose which claims read on the sum total of the elected species. Applicant ***must*** disclose which claims read **ONLY** on the elected "fluorescence quencher" (i.e., what groups read ONLY on Subgroup 18).

22. If applicant elects the invention of Group XI, applicant is ***further required*** to elect from the following patentably distinct species (note applicant must also elect Species in Subgroups 1-5 in paragraph 12). Claim 1 is generic.

Subgroup 19: Species of distinguishable characteristic (see claim 28)

A ***specific single species*** *of* distinguishable characteristic must be elected for the purposes of a search. Furthermore, applicant ***must*** disclose which claims read on the elected "distinguishable characteristic." Applicant ***must not*** group all elected species together (i.e., Subgroups 1-24) and then disclose which claims read on the sum total of the elected species. Applicant ***must*** disclose which claims read **ONLY** on the elected "distinguishable characteristic" (i.e., what groups read ONLY on Subgroup 19).

23. If applicant elects the invention of Group XIV, applicant is ***further required*** to elect from the following patentably distinct species (note applicant must also elect Species in Subgroups 1-5 in paragraph 12). Claim 1 is generic.

Subgroup 20: Species of stain (see claim 30)

A ***specific single species*** *of* stain must be elected for the purposes of a search. Furthermore, applicant ***must*** disclose which claims read on the elected "stain." Applicant ***must not*** group all elected species together (i.e., Subgroups 1-24) and then disclose which claims read on the sum total of the elected species. Applicant ***must*** disclose which claims read **ONLY** on the elected "stain" (i.e., what groups read ONLY on Subgroup 20).

24. If applicant elects the invention of Group XV, applicant is ***further required*** to elect from the following patentably distinct species (note applicant must also elect Species in Subgroups 1-5 in paragraph 12). Claim 1 is generic.

Subgroup 21: Species of markers (see claim 31)

A ***specific single species*** *of* markers must be elected for the purposes of a search. Furthermore, applicant ***must*** disclose which claims read on the elected "markers." Applicant ***must not*** group all elected species together (i.e., Subgroups 1-24) and then disclose which claims read on the sum total of the elected species. Applicant ***must*** disclose which claims read **ONLY** on the elected "markers" (i.e., what groups read ONLY on Subgroup 21).

Subgroup 22: Species of epitope expression (see claims 33-34)

A. Epitope expressed from an engoenous nucleic acid sequence
B. Epitope expressed from an exogenous nucleic acid sequence

25. If applicant elects the invention of Group XVII, applicant is ***further required*** to elect from the following patentably distinct species (note applicant must also elect Species in Subgroups 1-5 in paragraph 12). Claim 1 is generic.

Subgroup 23: Species of enzymes (see claim 39)

A ***specific single species*** *of* enzymes must be elected for the purposes of a search. Furthermore, applicant ***must*** disclose which claims read on the elected "enzymes." Applicant ***must not*** group all elected species together (i.e., Subgroups 1-24) and then disclose which claims read on the sum total of the elected species. Applicant ***must*** disclose which claims read **ONLY** on the elected "enzymes" (i.e., what groups read ONLY on Subgroup 23).

26. If applicant elects the invention of Group XVIII, applicant is ***further required*** to elect from the following patentably distinct species (note applicant must also elect Species in Subgroups 1-5 in paragraph 12). Claim 1 is generic.

Subgroup 24: Species of agent (see claim 41)

For the purposes of search, applicant is required to elect a ***single species*** of "agent" in step "1a" of claim 1 wherein a ***specific structure*** is set forth, which clearly shows all of the atoms and bonds that are necessary to define the agent including ***everything the agent comprises*** and including all attachment points including all atoms and bonds for the "linker" moiety if present. Applicant should ***not*** use notations like X or R when identifying the elected structure because these letters represent groups with variable members and, as a result, more than one species would be erroneously elected. Furthermore, applicant ***must*** disclose which claims read on the elected "agent." Applicant ***must not*** group all elected species together (i.e., Subgroups 1-24) and then disclose which claims read on the sum total of the elected species. Applicant ***must*** disclose which claims read **ONLY** on the elected "agent" (i.e., what groups read ONLY on Subgroup 24).

27. If applicant elects the invention of Group XXII-XXXIV, applicant is ***further required*** to elect from the following patentably distinct species (note applicant must also elect Species in Subgroups 1-5 in paragraph 12). Claim 1 is generic.

Subgroup 25: Species of transport protein (see claim 50)

A ***specific single species*** *of* transport protein must be elected for the purposes of a search. Furthermore, applicant ***must*** disclose which claims read on the elected "transport protein." Applicant ***must not*** group all elected species together (i.e., Subgroups 1-24) and then disclose which claims read on the sum total of the elected species. Applicant ***must*** disclose which claims read **ONLY** on the elected "transport protein" (i.e., what groups read ONLY on Subgroup 25).

Subgroup 26: Species of joining test compound to reporter (see claims 55-58)

A. Test compound is directly joined to the reporter via a chemical bound
B. A linker joins the test compound and reporter
C. A cleavable linker joins the test compound and reporter

Subgroup 27: Species of reporter (see claim 59)

A. Fluorophore
B. Chromophore
C. Radioisotope
D. Magnetic particle
E. Mass label
F. Spin label

In addition to the general class of reporters listed above, applicant is also required to elect for purposes of search a ***single species*** of "reporter" in step "1a" of claim 1 wherein a ***specific structure*** is set forth, which clearly shows all of the atoms and bonds that are necessary to define the reporter including ***everything the reporter comprises*** and including all attachment points including all atoms and bonds for the "linker" moiety if present. Applicant should ***not*** use notations like X or R when identifying the elected structure because these letters represent groups with variable members and, as a result, more than one species would be erroneously elected. Furthermore, applicant ***must*** disclose which claims read on the elected "reporter." Applicant ***must not*** group all elected species together (i.e., Subgroups 1-24) and then disclose which claims read on the

sum total of the elected species. Applicant ***must*** disclose which claims read **ONLY** on the elected "reporter" (i.e., what groups read ONLY on Subgroup 24).

Subgroup 28: Species of detection step (see claim 61)

A ***specific single species*** *of* detection step must be elected for the purposes of a search. Furthermore, applicant ***must*** disclose which claims read on the elected "detection step." Applicant ***must not*** group all elected species together (i.e., Subgroups 1-24) and then disclose which claims read on the sum total of the elected species. Applicant ***must*** disclose which claims read **ONLY** on the elected "detection step" (i.e., what groups read ONLY on Subgroup 28).

28. If applicant elects the invention of Group XXXV, applicant is ***further required*** to elect from the following patentably distinct species (note applicant must also elect Species in Subgroups 1-5 in paragraph 12). Claim 1 is generic.

Subgroup 26: Species of cells (see claim 53)

A ***specific single species*** *of* cells must be elected for the purposes of a search. Furthermore, applicant ***must*** disclose which claims read on the elected "cells." Applicant ***must not*** group all elected species together (i.e., Subgroups 1-24) and then disclose which claims read on the sum total of the elected species. Applicant ***must*** disclose which claims read **ONLY** on the elected "cells" (i.e., what groups read ONLY on Subgroup 23).

29. The species are distinct, each from the other, because their structures and modes of action are different. They would also differ in their reactivity and the starting materials from which they are made. For different species of method, the method steps for each species would differ. Moreover, the above species can be separately classified. Therefore, the species have different issues regarding patentability and represent patentably distinct subject matter.

30. Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

31. Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

32. Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

33. Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

34. Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143). Because the above restriction/election requirement is complex, a telephone call to applicants to request an oral election was not made. See MPEP § 812.01.

35. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

36. Applicant is also reminded that a 1 - month (not less than 30 days) shortened statutory period will be set for response when a written requirement is made without an action on the merits. This period may be extended under the provisions of 37 CFR 1.136(a). Such action will not be an "action on the merits" for purposes of the second action final program, see MPEP 809.02(a).

37. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D. Epperson, Ph.D. whose telephone number is (703) 308-2423. The examiner can normally be reached on Monday-Friday from 8:30 a.m. to 4:30 p.m..

38. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane, can be reached on (703) 308-4537. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Jon D. Epperson, Ph.D.
7/17/2002

BENNETT CELSA
PRIMARY EXAMINER